

**PREDICTORS OF MORTALITY AMONG  
HOSPITALIZED CHILDREN AGED 2 TO LESS THAN  
60 MONTHS WITH SEVERE AND VERY SEVERE  
PNEUMONIA IN URBAN TERTIARY REFERRAL  
HEALTH CARE**

*Dissertation submitted to*

**THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY**

*In partial fulfilment of the regulations*

*for the award of degree of*

**M.D DEGREE (PEDIATRICS) BRANCH VII**



**INSTITUTE OF CHILD HEALTH AND  
HOSPITAL FOR CHILDREN  
MADRAS MEDICAL COLLEGE**

**APRIL 2012**

## **CERTIFICATE**

This is to certify that the dissertation titled, “Predictors of mortality among hospitalized children aged 2 to < 60 months with severe and very severe pneumonia in urban tertiary referral health care” submitted by, Dr.Loganayaki R, to the Faculty of Pediatrics, The Tamilnadu Dr.M.G.R Medical University, Chennai, in partial fulfilment of the requirements for the award of M.D. Degree (Pediatrics) is a bonafide research work carried out by her under our direct supervision and guidance, during the academic year 2009-2011.

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This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulations for the M.D. Degree Examination in Pediatrics.

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dated:

The Institutional Review Board [Ethical committee] of Institute of Child Health and Hospital for Children, Chennai-08, was held on 30.01.2010 at 10.00AM at the Deputy Superintendents chamber.

**Members Present:** Dr.R.Kulandai Kasthuri  
Chair Person.

**Members:** 1. Dr.K.Gita  
2. Dr.P.Jeyachandran  
3. Dr.D.Vijaya Sekaran  
4. Prof.Girija Shyam Sundar  
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**Member Secretary:** Dr.Luke Ravi Chellaiah

**Title:** "Predictors of Need for Ventilation and Mortality among Hospitalized  
Children with Severe Pneumonia aged 2months – 59months in Urban  
Tertiary Health Care".

The Institutional Review Board was satisfied with the revised format  
submitted by you. Hence the Institutional Review Board is pleased to approve the  
study.

To,  
Dr.R.Loganayaki,  
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Director and Superintendent.

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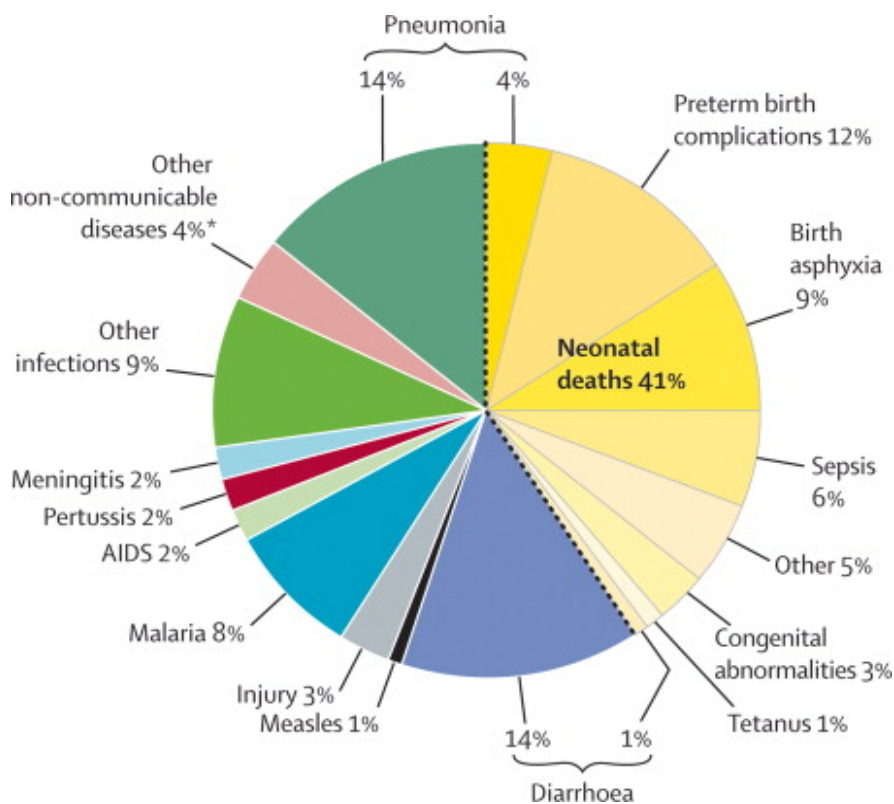
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## INTRODUCTION

Pneumonia, a pandemic killer is an inflammation of the parenchyma of the lungs. Although most cases of pneumonia are caused by microorganisms, non infectious causes include aspiration of food or gastric contents, foreign bodies, hydrocarbons, lipid substances and drug or radiation induced pneumonia<sup>[1]</sup>. For those pneumonias caused by non infectious agents the term pneumonitis is preferred.

## EPIDEMIOLOGY



Pneumonia is a substantial cause of morbidity and mortality among children < 5 yr of age throughout the world. Recent estimates from the World Health Organization suggest that pneumonia is responsible for 19% of deaths in the above age group, leading to 3 million deaths per year. Of these deaths, two thirds occur during infancy and more than 90% occur in the developing countries<sup>[2,3]</sup>. [In India, recent estimates in under-fives suggest that 13% of deaths and 24% of National Burden of Disease is due to pneumonia<sup>[4]</sup>. Hospital based studies have reported that 20–30% of admissions in under-fives are due to pneumonia. Case fatality rates in hospitalized children are reported to be between 8.7–47% <sup>[5-8]</sup>.

About 156 million new episodes of childhood clinical pneumonia occurred globally in 2000, more than 95% of them in developing countries. Various interventions have been done by the World Health Organization (WHO) to reduce pneumonia related morbidity and mortality. And it initiated the Acute Respiratory Infection (ARI) control program in 1983, which includes identification of children with pneumonia by clinical features (rapid respiration and difficulty in breathing) and administration of antimicrobials with a presumption that majority of pneumonia in developing countries are

because of bacterial pathogens, which led to a decline in the infant mortality rate by 10.7 (4.8–16.7) deaths per 1000 live births and decline in the mortality of under-fives by 36 deaths per 1000 live births<sup>[9]</sup>. A publication of Recent Child Health Epidemiology Reference Group (CHERG) of WHO and UNICEF estimates that as of 2008, 18 % of under five deaths were estimated to occur due to pneumonia i.e. 1.575 million deaths<sup>[10]</sup>. Of the WHO regions India contributes 23.5% of all pneumonia deaths in the world and tops the list. Case fatality rate for clinical pneumonia is 1.955 and that for severe pneumonia is 9.9%<sup>[11]</sup>.

### **WHO definition of very severe and severe pneumonia**

**Very severe pneumonia** is defined as cough or difficulty breathing with respiratory rate more than age specific cut off and at least one of: cyanosis, severe respiratory distress, inability to drink or vomiting or lethargy/unconsciousness/convulsions.

**Severe pneumonia** is defined as cough or difficulty breathing with respiratory rate more than age specific cut off plus one of: lower chest indrawing, nasal flaring, grunting.

A respiratory rate of 5 is reduced from cut off values for children with severe acute malnutrition.

### **Why are children vulnerable?**

A healthy child has many natural defenses that protect its lungs from the invading pathogens that cause pneumonia. However children and infants with compromised immune systems have weakened defenses. Undernourished children, particularly those not exclusively breast fed or with inadequate zinc intake, pre-existing illnesses, such as symptomatic HIV infections and measles, are more likely to develop pneumonia.

### **ETIOLOGY**

Childhood clinical pneumonia is caused by a combination of exposure to risk factors related to the host, the environment and infection.

**Risk factors related to the host and the environment that affect incidence of childhood clinical pneumonia in the community in developing countries<sup>[11]</sup>.**

**Definite risk factors**

Malnutrition (weight-for-age z-score  $< -2$ )

Low birth weight ( $\leq 2500$  g)

Non-exclusive breastfeeding (during the first 4 months of life)

Lack of measles immunization (within the first 12 months of life)

Indoor air pollution

Crowding

**Likely risk factors**

Parental smoking

Zinc deficiency

Mother's experience as a caregiver

Concomitant diseases (e.g. diarrhea, heart disease, asthma)

**Possible risk factors**

Mother's education

Day-care attendance

Rainfall (humidity)

High altitude (cold air)

Vitamin A deficiency

Birth order

Outdoor air pollution

## **CLASSIFICATION**

Pneumonia can be classified in several ways.

**A)** Early classification descriptions of pneumonia focused on the **anatomic or pathologic appearance** of the lung, either by direct inspection at autopsy or by its appearance under a microscope.

- A lobar pneumonia is an infection that only involves a single lobe, or section, of a lung. Lobar pneumonia is often due to *Streptococcus pneumoniae* (though *Klebsiella pneumoniae* is also possible).
- Multilobar pneumonia involves more than one lobe, and it often causes a more severe illness.
- Bronchial pneumonia affects the lungs in patches around the tubes (bronchi or bronchioles).

- Interstitial pneumonia involves the areas in between the alveoli, and it may be called "interstitial pneumonitis." It is more likely to be caused by viruses or by atypical bacteria.

#### **B) Combined clinical classification:**

Classified pneumonia by clinical characteristics, into "acute" (<3 weeks duration) and "chronic" pneumonias. This is useful because chronic pneumonias tend to be either non-infectious, or mycobacterial, fungal, or mixed bacterial infections caused by airway obstruction.

#### **C) Newer classification:**

- **Community acquired pneumonia (CAP)** the most common type, is an acute infection of the pulmonary parenchyma in a previously healthy child, acquired outside of a hospital setting. The patient should not have been hospitalized within 14 days prior to the onset of symptoms or has been hospitalized less than 3 days prior to onset of symptoms. Overall, *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia worldwide. The term "walking pneumonia" has been used to describe a type of community-acquired pneumonia of

less severity (because the sufferer can continue to "walk" rather than require hospitalization).

- **Hospital-acquired Pneumonia:** Also called nosocomial pneumonia, is pneumonia acquired during or after hospitalization for another illness or procedure with onset at least 72 hrs after admission. Ventilator-associated pneumonia (VAP) is a subset of hospital-acquired pneumonia. VAP is pneumonia which occurs after at least 48 hours of intubation and mechanical ventilation.
- **Healthcare-associated pneumonia:** Those patients living outside the hospital who have recently been in close contact with the health care system developing pneumonia.

#### **D) Other types of pneumonia :**

- **Severe acute respiratory syndrome (SARS)** SARS is a highly contagious and deadly type of pneumonia which first occurred in 2002 after initial outbreaks in China. SARS is caused by the corona virus.
- **Bronchiolitis obliterans organizing pneumonia (BOOP)** also known as cryptogenic organizing pneumonitis (COP), is caused by inflammation of the small airways of the lungs.



- Eosinophilic pneumonia is invasion of the lung by eosinophils, often occurs in response to infection with a parasite or after exposure to certain types of environmental factors.
- Chemical pneumonia is caused by chemical toxicants such as pesticides, which may enter the body by inhalation or by skin contact. When the toxic substance is an oil, the pneumonia may be called lipoid pneumonia.
- Aspiration pneumonia is caused by aspirating foreign objects which are usually oral or gastric contents, either while eating, or after reflux or vomiting which results in bronchopneumonia.

**D) WHO classification:** Pneumonia in children may additionally be classified based on signs and symptoms as non-severe, severe, or very severe. [\[12\]](#)

## E ) AETIOLOGICAL CLASSIFICATION

Age	Bacterial pathogens	Viral pathogens	Others
Neonates	Group B streptococcus, gram negative bacilli(E.coli, Kleb pneumonia), stap aureus	RSV, Herpes simplex, Cytomegalovirus, Adenovirus	
1-3 months	Streptococcus pneumonia, H influenza type b	RSV	Chlamydia trachomatis
4-60 months	Streptococcus pneumonia, H influenza type b	Parainfluenza 1& 3, Adenovirus, influenza virus A& B	Mycoplasma pneumonie

Evidence of a potential causative agent has been identified in 24-85% of the cases. In a recent study from India etiological agents could be identified in 94% of the patients. Bacterial etiology was demonstrated in 16%, viruses in 38%, mycoplasma in 24% and Chlamydia pneumonie in 11% of the cases. Mixed infection was present in 8%<sup>[13]</sup>. Other studies from India have demonstrated the following as the proportion of the organisms in pneumonia in children 2-60months of age viruses- 38%, bacteria-62.6%, mycoplasma– 24-

30%, chlamydia- 6-11%, mixed infections- 9%.%<sup>[14-16]</sup> · (Bacterial causes: S pneumoniae–33-40%, H influenzae b–22 %)

Fungal pneumonia is uncommon, but it may occur in individuals with immune system problems due to AIDS, immunosuppressive drugs, or other medical problems. The pathophysiology of pneumonia caused by fungi is similar to that of bacterial pneumonia. Fungal pneumonia is most often caused by *Histoplasma capsulatum*, *blastomyces*, *Cryptococcus neoformans*, *Pneumocystis jiroveci*, and *Coccidioides immitis*.

### **Pathogenesis:**

The lower respiratory tract is normally kept sterile by physiologic defense mechanisms, including the mucociliary clearance, the properties of normal secretions such as secretory immunoglobulin A and clearing of the airway by coughing. Immunologic defense mechanisms of the lung that limit invasion by pathogenic organisms include macrophages present in alveoli and bronchioles, secretory IgA and other immunoglobulins.

Viral pneumonia usually results from spread of infection along the airways, accompanied by direct injury of the respiratory

epithelium resulting in airway obstruction from swelling, abnormal secretions, and cellular debris. The small caliber of airways in young infants makes them particularly susceptible to severe infection. Atelectasis, interstitial edema,, and ventilation perfusion mismatch causing significant hypoxemia often accompany airway obstruction. It can also predispose to secondary bacterial infection by disturbing normal host defense mechanisms, altering secretions and modifying the bacterial flora.

When bacterial infection is established in the lung parenchyma, the pathologic process varies according to the invading organism. *Streptococcus pneumoniae* produces local edema that aids in the proliferation of organisms and their spread into adjacent portions of lung often resulting in the characteristic lobar involvement.

*S. aureus* pneumonia manifests in confluent bronchopneumonia which is often unilateral and characterized by presence of extensive areas of hemorrhagic necrosis and irregular areas of cavitation of the lung parenchyma, resulting in pneumatoceles, empyema or at times bronchopulmonary fistulas.

*Mycoplasma pneumoniae* attaches to the respiratory epithelium, inhibits ciliary action and leads to cellular destruction and an inflammatory response in the submucosa. As the infection progresses, sloughed cellular debris, inflammatory cells, and mucus cause airway obstruction, with spread of infection occurring along the bronchial tree as it does in viral pneumonia.

## **INVESTIGATION**

Chest X ray are usually not needed in those assigned to domiciliary care. Indications for chest X ray are

- If diagnosis of child under five years with fever of 39 c of unknown origin
- If complication (eg pleural effusion) suspected
- Ambiguous features, unresponsive to treatment even after 48 hours of therapy/ deteriorates
- For follow up of children with lobar collapse or ongoing symptoms

Routine microbiological test are of no use. Acute phase reactants like CRP, TLC are not diagnostic, but may be useful to response to treatment. Small effusions can be picked up by ultrasonogram. Pleural tap is indicated only if the collection is > 10 mm on sonogram

## **TREATMENT**

For very severe pneumonia the child should be admitted in hospital and start on oxygen, maintenance IV fluids and antibiotics. Obtain a chest x ray. Oxygen must be given through appropriate device at correct concentration to those with hypoxemia( $SpO_2 < 92\%$ ) or with severe chest indrawing or when respiratory rate is  $> 70/\text{minute}$ . Give ampicillin 50mg/kg IV every 6<sup>th</sup> hourly and gentamycin 7.5mg/kg IV OD. If the child responds well discharge after 5 days to continue treatment at home with oral amoxicillin(15mg/kg/dose tds) for 5 days. If the child does not improve by 48 hours to the above treatment reassess for complications and switch to inj ceftriaxone(80mg/kg OD) for 10 days. Consider supportive measures

like antipyretics, bronchodilators if wheeze is present and suctioning. Watch for complications.

Staphylococcal pneumonia is suspected if there is rapid progression of disease or pneumatocele/ pneumothorax/ effusion on chest x ray or child has large skin boil, abscess, infected scabies, post measles pneumonia which is not responding within 48 hours to initial therapy. Consider adding anti staphylococcal drugs.

In a healthy child with severe pneumonia can treated with domiciliary care with oral amoxicillin for a period of 5-7 days. The mother is explained about the danger signs and advised to return immediately if any appears. Whereas any child with abnormal chest x ray/ complications, severe acute malnutrition, associated illnesses, mother not confident to take care in home, admit and treat with oxygen, IV antibiotics and maintenance IV fluids as necessary

## **PLEURAL EFFUSION AND EMPYEMA**

A child with severe or very severe pneumonia should be suspected to have effusion or empyema if one of the following is present.

- Evidence of staphylococcal infection in the form of impetigo/abscess
- Chest pain, fullness of intercostals spaces, diminished breath sounds, dull note on percussion and fever persists despite antibiotics for > 48 hours.

A chest x ray must be taken to confirm along with diagnostic pleural tap. Send the fluid specimen for analysis.

All empyema should be treated with drainage of pleural cavity by intercostals drainage with under water seal. And add anti staphylococcal drugs for 7-10 days. When the child improves continue with cloxacillin orally for a minimum period of 3 weeks.



**Clinical and radiographical clues to the etiological diagnosis of pneumonia**<sup>[17]</sup>

<b>Radiological finding</b>	<b>Clinical circumstance</b>	<b>Organism</b>
Segmental consolidation	Community-acquired	S pneumoniae, M pneumoniae –Lobar
Consolidation	Community-acquired	S pneumoniae
Rounded pneumonia	Community-acquired	S pneumoniae
Interstitial pneumonia	Community-acquired	(winter) Virus, Mycoplasma pneumoniae
Cavitation/necrosis	Aspiration Post measles,	S aureus, Gram negative bacilli, anaerobes, actinomycosis
Multiple cavitary nodules, pneumatoceles	malnourished	S aureus
Empyema	Complication of pneumonia	S pneumoniae S aureus, Gram negative bacilli
Lymphadenopathy		Mycoplasma pneumoniae, M tuberculosis

## WHO response

In 2009, WHO and UNICEF launched the *Global action plan for the prevention and control of pneumonia* (GAPP). The aim is to accelerate pneumonia control with a combination of interventions to protect, prevent, and treat pneumonia in children.

### FRAMEWORK FOR PNEUMONIA PREVENTION:

- Adequate nutrition, EBF for first 6 months of life.
- Vitamin and zinc supplementation.
- Treating associated illnesses appropriately.
- Well ventilated home.
- Good indoor environment.
- Encouraging good hygiene in crowded homes.
- Vaccination against Hib, pneumococcal, measles and influenza if possible



## REVIEW OF LITERATURE

1. **Tiewosh K, et al<sup>[18]</sup>** did a nested case control study among 200 children hospitalized with severe pneumonia aged below 5 years as defined by WHO to determine the factors predicting the outcome. They concluded who had not got exclusive breast feeding, who had lived in an overcrowded homes, altered sensorium, pallor, head nodding, abnormal leukocyte counts were associated with mortality. Factors like lack of exclusive breast feeding, abnormal chest x ray, overcrowding were identified as determinants for prolonged hospital stay.
2. **Seghal V, et al<sup>[7]</sup>** conducted a prospective cohort study in tertiary care hospital to identify the predictors of mortality due to acute lower respiratory tract infection. Significant independent predictors of mortality were age less than 1 year, weight for age Z score < -3, associated loose stools, inability to feed. The case fatality rate was severe pneumonia 8.7 % and very severe pneumonia 47%.
3. **Banajeh SM, et al<sup>[13]</sup>** from Yemen have studied prospectively 529 children aged below 5 years hospitalized for severe

pneumonia, to define their clinical characteristics and to identify risk factors associated with death from pneumonia. They found age less than 1 year, weight for age < 60 %, Hb < 10 g%, cyanosis, heart failure were associated with an increased risk of dying from severe pneumonia.

4. **Shah V, et al<sup>[19]</sup>** did a case control study in 400 children hospitalized with severe pneumonia aged below five years at tertiary care hospital in south Kerala to identify the risk factors for severe pneumonia as ascertained by WHO criteria and concluded that young age, overcrowding, malnutrition, poor immunization were the factors emerged as significant risk factors. Also they observed low parental education, environmental pollution, discontinuation of breast feeding in young infants, malnutrition, low birth weight were the significant factors in univariate analysis. And concluded as correction of these factors can probably reduce mortality due to acute respiratory infections.

5. **Suwanjutha S, et al<sup>[20]</sup>** conducted a prospective study among Thai children under 5 years hospitalized with severe

pneumonias to identify the risk factors associated with morbidity and mortality of pneumonia. From univariate analysis they found predictors on admission to predict fatal outcome were rapid respiratory rate > 50/ minute, gallop rhythm and cyanosis.

6. **Shaan, et al**<sup>[21]</sup> did a prospective study among 748 children in Papua New Guinea who had severe pneumonia, as defined by the World Health Organization in a tertiary health care setup, to identify children who have a high risk of dying from pneumonia so that these children can be given more intensive therapy. They observed there was a very high mortality in children with a prolonged illness, severe roentgenogram changes, cyanosis, leukocytosis, hepatomegaly or inability to feed, and there was a trend toward a higher mortality in children with grunting or severe chest in drawing.

7. **Laura L Jones, et al**<sup>[22]</sup>, provided an update on the importance of association between passive smoking and lower respiratory tract infections. They identified 60 studies suitable for inclusion in the meta-analysis and results were smoking by either parent or other household members significantly increased the risk of

LRI; odds ratios (OR) were 1.22 (95% CI 1.10 to 1.35) for paternal smoking, 1.62 (95% CI 1.38 to 1.89) if both parents smoked, and 1.54 (95% CI 1.40 to 1.69) for any household member smoking. Pre-natal maternal smoking (OR 1.24, 95% CI 1.11 to 1.38) had a weaker effect than post-natal smoking (OR 1.58, 95% CI 1.45 to 1.73). They concluded as passive smoking in the family home has got a major influence on the risk of lower respiratory infection in infants. Risk is particularly strong in relation to post natal maternal smoking.

8. **Victoria, CG *et al***<sup>[23]</sup> from Brazil have studied prospectively the children admitted in a tertiary care hospital with severe pneumonia with radiological confirmation, to investigate the risk factors for pneumonia. They identified the incidence of radio logically confirmed pneumonia was associated with low birth weight, low weight for age, lack of breast feeding, young maternal age and who live in crowded homes. They concluded saying, actions directed against the above risk factors may help prevent the major cause of deaths of children younger than 5 years.

9. **Fonseca W, et al**<sup>[25]</sup> carried out a case control study in 650 hospitalized children who presented with clinical picture of severe pneumonia with radiological confirmation. Cases and controls were compared with respect to a variety of socio demographic, environmental, reproductive, nutritional and morbidity factors. They observed low birth weight, non breast feeding, crowding, high parity, and incomplete vaccination status were the risk factors increasingly associated with childhood pneumonia.
10. **Deivanayagam N, et al**<sup>[26]</sup> conducted a case control study at tertiary care hospital to identify the risk factors for death among hospitalized children with pneumonia. By univariate analysis they found the risk factor for death in pneumonia observed were severe pneumonia, malnutrition, age less than 6 months.
11. **Bonadio WA, et al**<sup>[17]</sup> from Milwaukee did a retrospective analysis of 86 consecutive cases of childhood pneumonia with clinical features indicative of bacterial etiology . All patients had temperature greater than or equal to 40 degrees C, a lobar pulmonary infiltrate on chest radiograph, and a peripheral white blood cell concentration greater than 20,000/mm<sup>3</sup> or absolute

band count greater than 2,000/mm<sup>3</sup>. Only one of 86 patients had a bacterial pathogen isolated by blood culture (*Haemophilus influenzae*, type b). Though the clinical findings and laboratory data seems to be insensitive markers for distinguishing those with concomitant bacteremia, these abnormal clinical picture carries increase risk of severity in childhood pneumonia.

12. **I.G.G.Djelantik, et al**<sup>[27]</sup> from Indonesia conducted a Prospective study to identify predictive factors for mortality in subjects hospitalized with severe pneumonia in rural developing country setting. The study population was 4351 children. Of these 12% died during the study period. They observed case fatality proportions were seasonal, with peaks occurring immediately after peaks in the proportion of cases positive for respiratory syncytial virus. Children with an oxygen saturation  $\leq 85\%$  or age younger than 4 months were 5.6 times more likely to die than children with none of these predictive factors (95 per cent CI, 4.5-7.1) . They found significant independent factors were age < 4 months with relative risk of 3.5, temperature  $\leq 36^{\circ}\text{C}$  (relative risk 2.2), Wheezing with relative risk of 1.2,



Hemoglobin <7g (relative risk 2.2), abnormal chest x ray, hypoxemia.

13. **Suzuki M, et al**<sup>[28]</sup> conducted a population-based large-scale cross-sectional survey covering all residents of 33 communes in Khanh Hoa Province, the central part of Vietnam, to find out the association of environmental tobacco smoking exposure with an increased risk of hospital admissions for pneumonia in children under 5 years of age in Vietnam. A total of 353 525 individuals living in 75 828 households were identified in the study areas. Of these, 24 781 (7.0%) were aged <5 years. The prevalence of environmental tobacco smoking was 70.5% and the period prevalence of hospital admissions for pneumonia was 2.6%. Multiple logistic regression analysis showed that exposure to tobacco smoke as independently associated with hospital admissions for pneumonia (adjusted odds ratio 1.55, 95% CI 1.25 to 1.92). And they estimated that 28.7% of childhood pneumonia in their community was attributable to environmental tobacco smoking.

## **STUDY JUSTIFICATION**

- To achieve the Millennium Development goal of reducing under five mortality by two thirds by 2015 will require urgent action to reduce childhood pneumonia deaths, which account for 19% of all under five deaths. For that we should know which are all factors that favors the chances of mortality in our community. Hence the plan of management can be targeted effectively.
- To identify the trends of predictive factors in hospitalized children with severe pneumonia and this is likely to reflect trends in pneumonia mortality in our community. This will also have bearing in evaluation of interventions like Integrated Management of Neonatal and Childhood Illnesses(IMNCI) and Universal Immunisation on proposal to newer vaccines .

## **AIM OF THE STUDY**

To find out the predictive factors of mortality among children aged 2 months to < 60 months hospitalized with severe and very severe pneumonia with radiological confirmation

## **SUBJECTS AND METHODS**

**STUDY DESIGN :** Descriptive / Nested case control study

**STUDY PERIOD :** December 2009 – October 2011

**STUDY PLACE :** Medical wards and Pediatric intensive care unit,  
Institute of child health and hospital for children,  
Chennai

**STUDY POPULATION :** Children admitted with signs and symptoms of severe and very severe pneumonia in general medical wards and pediatric intensive care unit of ICH & HC, Egmore, Chennai.

**i) Cases:** All children fulfilling the inclusion criteria for severe and very severe pneumonia got admitted in our hospital and expired.

**ii) Controls:** All children who met the case definition of for very severe and severe pneumonia got admitted in our hospital and recovered.

**iii) Cases: Controls Ratio- 1: 3**

**iv) Sample size: 302**

**INCLUSION CRITERIA:**

All children in the age group of 2 months to < 60 months who meet the case definition of very severe and pneumonia confirmed by chest X ray And got admitted in the hospital during the study period are included in the study.

**Case definition:** Children presenting with fever/ cough and cold with

- difficulty in breathing having increased respiratory rate
  - $\geq 60$  /minute in children <2 months
  - $\geq 50$  /minute in 2-12months
  - $\geq 40$  /minute in 13-60 months
- Chest retractions and with or without any one of the following
  - Nasal flaring, grunt, cyanosis, inability to take feeds, altered sensorium
- And with chest X ray confirmed by radiologist

**EXCLUSION CRITERIA:**

Children with co-morbidities like acute CNS infection, chronic respiratory disease, confirmed pulmonary tuberculosis, h/o recurrent cough, primary immunodeficiency, AIDS, congenital heart disease, those with any associated life threatening illness, those who got

admitted in another hospital prior to presentation or whose parents did not accept to participate in this study were excluded.

## **MANOEUVRE**

The study was conducted in the pediatric wards and intensive care unit at the Institute of Child Health and Hospital for children, Chennai, which is an urban, tertiary care centre between December 2009 and October 2011. Children of either sex, between 2 months to < 60 months of age got admitted with pneumonia fulfilling the WHO criteria of severe and very severe pneumonia with chest X ray confirming the diagnosis were enrolled in less than 24 hours of admission. Parents of patients who met the criteria were called to participate in the study. After explaining about the study in detail and getting consent, a predesigned performa (annexure) was used to record the details of personal and demographic profile, clinical presentation, laboratory investigations, treatment and course in the hospital and the final outcome.

Overcrowding was determined by calculating how many family members stay per room<sup>[29]</sup>. Those who were not found to be in the following norm were labeled as staying in overcrowded house.

1 Room maximum 2 persons, or 2 Rooms maximum 3 persons, or 3 Rooms maximum 5 persons, or 4 Rooms maximum 7 persons, or 5 or more rooms maximum 10 persons (additional 2 for each further room).

The evidence for presence of passive smoking<sup>[22]</sup> was considered when any of the family member smokes in and around the home and who also handles the baby with nicotine stain still in their hands.

As the combustion of woods, charcoal, crop residues, kerosene pollutes the environment of indoor<sup>[30]</sup> and elevates the carboxyhemoglobin levels, which paves a way to contract the disease, cooking mode adopted by parents were enquired and recorded. The delivery mode, any insult in prenatal period and birth weight of the child was recorded. Details of breast feeding and addition of other feeds was recorded.

An infant who received only breast feeding in the first 6 months of life was considered to be exclusively breast fed, those who received two thirds of the calories from breast milk and also on some additional feeds were considered as on predominant breast feeds and those who are on artificial feeds / receiving breast feeds occasionally per day were called as non breast fed.

Status regarding immunization was assessed by verifying the immunization records or asking the parents. Practising the following ways were considered as bad child rearing techniques. Nose blowing, instilling oil in nose and ear, applying neem oil along with camphor, giving their own preparation on the name of so called herbal medicine, incense burning as a ritual, bottle feeds. Then their educational status and the reasons for their late health care seeking behavior were also noted. Nutritional status in children assessed by taking weight and height and values plotted using WHO's growth chart. The parameter weight for height is considered and when the Z score is  $\leq -3$  called as severe acute malnutrition, when it lies between  $-2$  to  $> -3$  called as moderate acute malnutrition, anything  $> -2$  taken as normal.

A detailed clinical examination was carried out at the first contact. A child presenting with heart rate above or below normal, poor peripheral perfusion along with or without normal blood pressure are documented as shock<sup>[31]</sup>. And later whether the shock responds to fluids / vasoactive agents are recorded and called as fluid refractory shock when the shock persists despite of infusing 60ml/kg bolus of isotonic fluid( or developing myocardial dysfunction with lesser bolus), requiring vasoactive agents. Presence of altered sensorium is considered referring to AVPU scale<sup>[32]</sup> used in emergency room



according to pediatric advanced life support guidelines. Oxygen saturation (SpO<sub>2</sub>) is measured at finger or toe with a pulse oxymeter using an appropriate sized pediatric sensor. The oxymetry measurement is recorded after stabilization of the reading for one minute. Hypoxemia is defined as SpO<sub>2</sub> <94% in room air<sup>[33]</sup>. Results of the investigations including hemoglobin, total leukocyte count [ $>10,000/\text{cmm}^3$  as leukocytosis,  $< 5000/\text{cmm}^3$  as leucopenia, in between taken as normal] chest x-ray, blood culture, pleural culture, liver function tests reports, serum creatinine, urine output in needed cases were recorded.

Chest radiographs were done in all the patients at first contact itself. The chest radiographs were read by the chief radiologist of our hospital and interpreted as normal or abnormal showing evidence of pneumonia/consolidation/ infiltrates/cysts/ pleural effusion. Multiorgan dysfunction syndrome was considered when any of the following is there.<sup>[34]</sup>

1. Cardiovascular dysfunction (after fluid resuscitation  $\leq 40$  ml/kg of crystalloid)-hypotension with blood pressure  $< 5$ th percentile for age or systolic blood pressure  $< 2$  standard deviations below normal for age, or vasopressor requirement or two of the following-oliguria (urine output  $< 0.5$  ml/kg/hr)/ prolonged

capillary refill > 5 seconds/ core to peripheral temperature difference > 3°C.

2. Respiratory dysfunction (in the absence of cyanotic heart disease or known chronic lung disease) -supplemental oxygen requirement of greater than  $\text{FiO}_2$  0.5 to maintain oxygen saturation  $\geq 92\%$
3. Neurologic dysfunction -Glasgow Coma Score (GCS)  $\leq 11$ , OR
4. Hematologic dysfunction -platelet count  $< 80,000/\text{mm}^3$  or 50% drop from maximum in chronically thrombocytopenic patients, or international normalized ratio (INR)  $> 2$  or Disseminated intravascular coagulation
5. Renal dysfunction -serum creatinine  $\geq 2$  times the upper limit of normal for age
6. Hepatic dysfunction -total serum bilirubin  $\geq 4$  mg/dl, OR alanine aminotransferase (ALT)  $\geq 2$  times the upper limit of normal.

## **STATISTICAL ANALYSIS**

The data collected were entered in an excel sheet and then transferred to SPSS software version 16.0 for statistical analysis. Chi Square test was used to study the associations between the predictive factors and the outcome. The significant factors derived from the bivariate analysis were studied separately using Odd's Ratio. To find out the independent significance of each factor towards the outcome, we used the multiple logistic regression analysis. The p value of  $< 0.05$  was considered statistically significant.

The study was approved by the Institutional Review Board, MMC, Chennai. A written informed consent was taken from the parents.

## **OBSERVATION**

A total of 302 children met the inclusion criteria and were enrolled in the study. Among these 194(64.2%) children had very severe pneumonia and 108(35.8%) children had severe pneumonia. Among these 80(26.5%) were infants less than 6 months of age, 95(31.5%) were infants between 7 -12 months, 65(21.5%) were between 13- 24 months, 25(8.3%) were between 25- 36 months and 37 (12.3%) were between 37- 60 months. The lowest age reported was 45 days. Mean age was 6.29 months. 161(53.3%) children were females and 141(46.7%) children were males, with female to male ratio of 1.1:1. [Table 1]

**Table 1. Age and sex distribution among those recovered and expired**

Age[months]	Expired group		Recovered group		Total n(%)
	Male n(%)	Female n(%)	Male n(%)	Female n(%)	
<b>2 - 6</b>	13(17.1)	17(22.4)	23(10.2)	27(11.9)	80(26.4)
<b>7 – 12</b>	12(15.8)	17(22.4)	33(14.6)	33(14.6)	95(31.5)
<b>13 – 24</b>	5(6.5)	4(5.2)	27(11.9)	29(12.8)	65(21.5)
<b>25 – 36</b>	2(2.6)	2(2.6)	8(3.5)	13(5.7)	25(8.3)
<b>37 - 60</b>	3(3.9)	3(3.9)	16(7.0)	15(6.6)	37(12.3)

**Hospital stay :**

- The mean hospital stay among expired group was 4.05 days  $\pm$  0.47 and among recovered group was 7.67 days  $\pm$  0.23. In our study we observed children in expired group stayed mostly for less than one day. . Among expired group 23(30.3%) stayed for one day, 33(43.4%) stayed for 2-4 days, 10(7.6%) stayed for 5-7 days. Only 2 children in mortality group stayed for quite long, 21 days.[Table 2]

**Table 2. Hospital stay duration among both groups**

Hospital stay	Expired group	Recovered group	P
	n(%)	n(%)	value
1 day	23(30.3)	2(0.8)	0.000
2-4 days	33(43.4)	29(12.8)	
5-7 days	10(13.2)	89(39.4)	
>1 week	2(2.6)	86(38.1)	

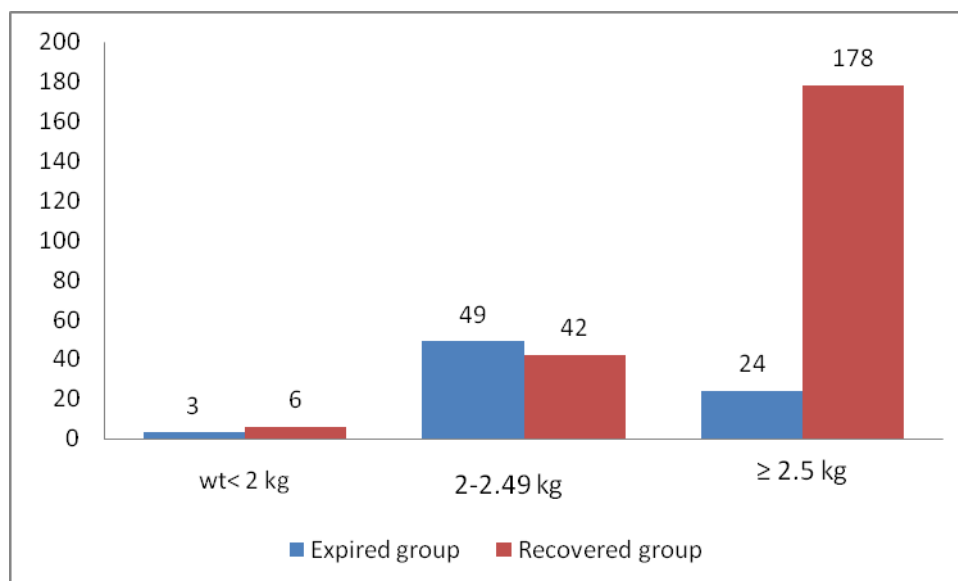
**Health seeking behavior Vs Outcome**

	Expired	Recovered	P
First medical contact	group n(%)	group n(%)	value
from illness			
< 48 hours	2(2.6)	17(7.5)	0.120
48-72 hours	53(69.7)	140(61.9)	
72-96 hours	20(26.3)	56(24.7)	
>96 hours	1(1.3)	13(5.7)	

In both groups care takers took more than 48 hours to contact health care from onset of medical illness which was not significant statistically.

### **Birth weight Vs Outcome**

Among expired group 64.5% children had birth weight between 2-2.49 kg whereas in recovered group only 18.6% had in that range. 31.6% children among expired group had birth weight more than or equal to 2.5 kg and 78.7% among recovered group.[Fig 1]



**Figure 1: Bar chart showing birth weight among expired and recovered groups**

**Table 3:Breast fed status Vs Outcome**

Breast fed status	OUTCOME		P value
	Expired n(%)	Recovered n(%)	
Exclusively fed upto 6 months	5(6.6)	49(21.7)	0.000
Predominantly fed	36(47.4)	162(71.7)	
Non breast fed	35(46.1)	15(6.6)	

Among expired group, only 6.6% children were exclusively breast fed upto first six months compared to 21.7% among recovered group. 46.1% children in expired group were on artificial feeds and 6.6% among recovered group.[Table 3]



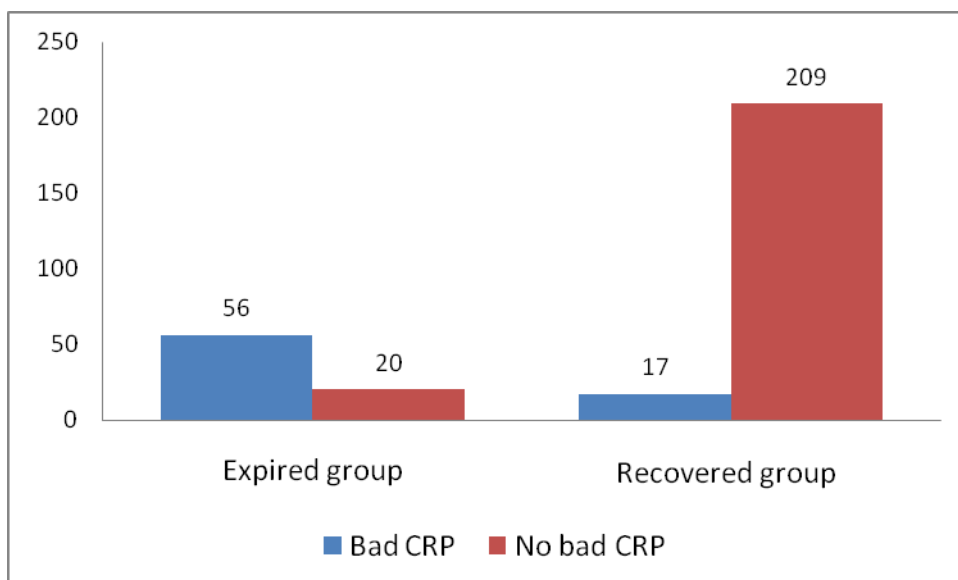
**Table 4: Mother's education status Vs Outcome**

<b>Maternal education</b>	<b>OUTCOME</b>		<b>P value</b>
	<b>Expired n(%)</b>	<b>Recovered n(%)</b>	
Illiterate	22(28.9)	32(14.2)	0.001
≤ 9 standard	41(53.9)	101(44.7)	
10-12 standard	13(17.1)	89(39.4)	
Graduate	0	4(1.8)	

Among expired group, 28.9% child's mother were illiterate, 53.9% studied below secondary level. Among recovered group only 14.2% were illiterate, 44.7% studied below secondary level , 39.4% completed secondary level and 1.8% were graduated.[Table 4]

## Bad child rearing practices Vs Outcome

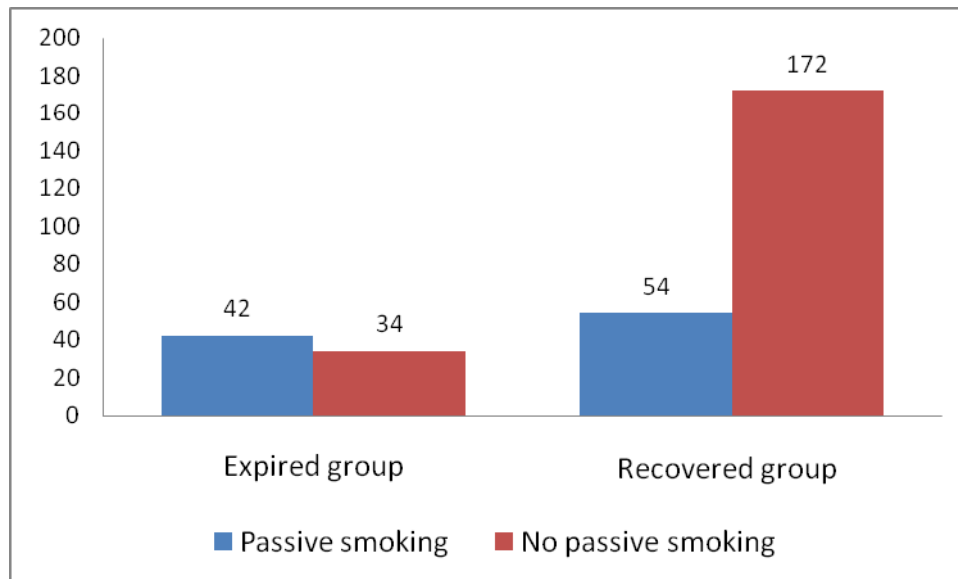
Around 73.6% children among expired group were reared by bad child rearing practices compared to only 7.5 % among recovered group. Bad child rearing practices[CRP] was 34 times more commonly observed among expired group when compared to recovered group. OR (95% CI) was 34.42(16.91-70.00) and p value was 0.000, significant.



**Figure 2: Showing bad child rearing practices among both groups**

### Passive smoking Vs Outcome

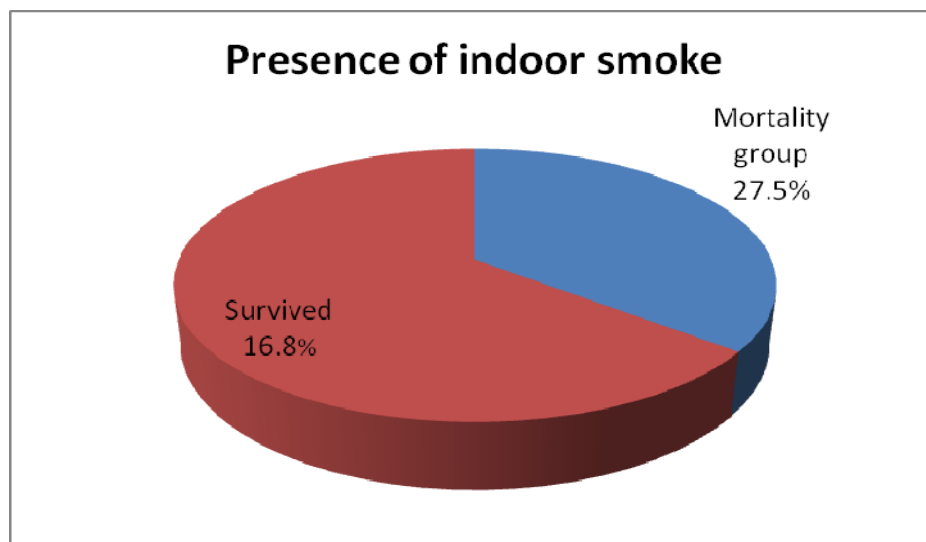
Around 55.2% children among expired group live environment polluted with tobacco smoke compared to only 23.8 % among recovered group. Passive smoking was 3.94 times more commonly observed among expired group when compared to recovered group. OR (95% CI) was 3.94(2.20-7.05) and p value was 0.000, significant.[Fig 3]



**Figure 3: Showing passive smoking among both groups.**

### Indoor smoke Vs Outcome

Around 27.6% children among expired group live in indoor polluted homes compared to only 16.8 % among recovered group. Indoor pollution was 1.9 times more commonly observed among expired group when compared to recovered group. OR (95% CI) was 1.9(1.03-3.5) and p value was 0.04, significant.[Fig 4]



**Figure 4: Pie chart showing presence of indoor smoke among expired and recovered groups.**

### Overcrowding Vs Outcome

Among expired group 31.6% children live in crowded homes and 30.5% among recovered group. We did not observe any statistical significance among them.

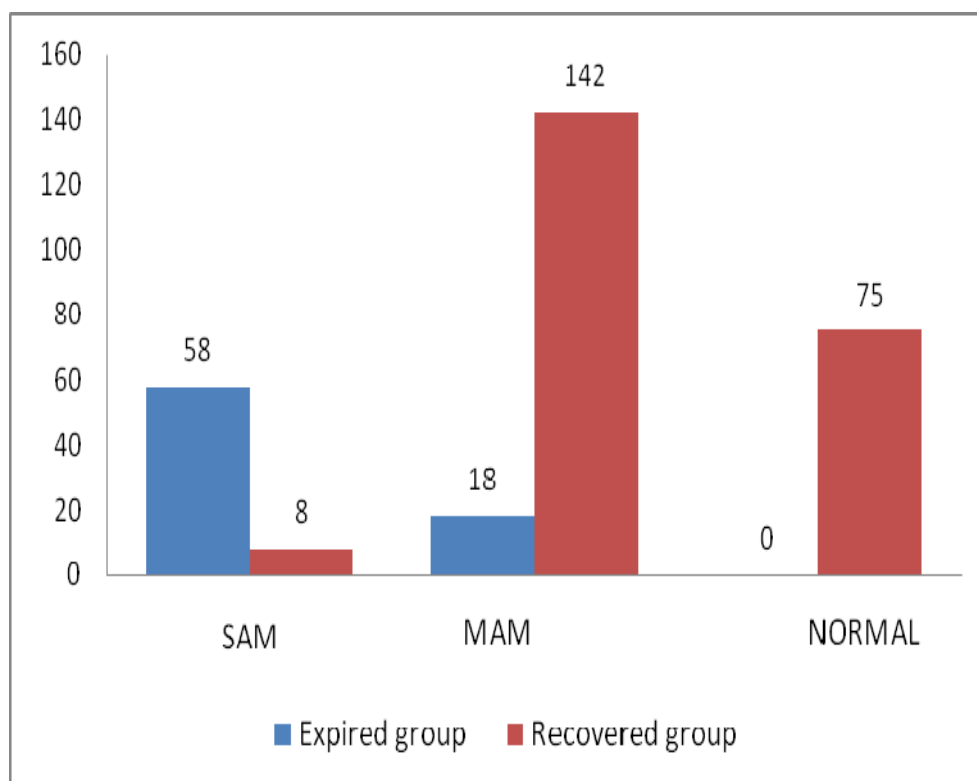
**Table 5: Measles immunization Vs Outcome**

Measles immunization	OUTCOME		TOTAL
	Expired n(%)	Recovered n(%)	
Not immunised	55(72.3)	107(47.3)	67
Immunized	21(27.6)	119(52.6)	235
<b>TOTAL</b>	76	226	302
OR(95% CI) =2.91(1.6-5.4) p value is 0.000			

Among expired group 72.3% were not vaccinated with measles vaccine whereas only 47.3 were not vaccinated in recovered group. Children who were not immunised with measles vaccine were 2.9 times more likely to die of severe/ very severe pneumonia.[Table 5]

## Malnutrition Vs Outcome

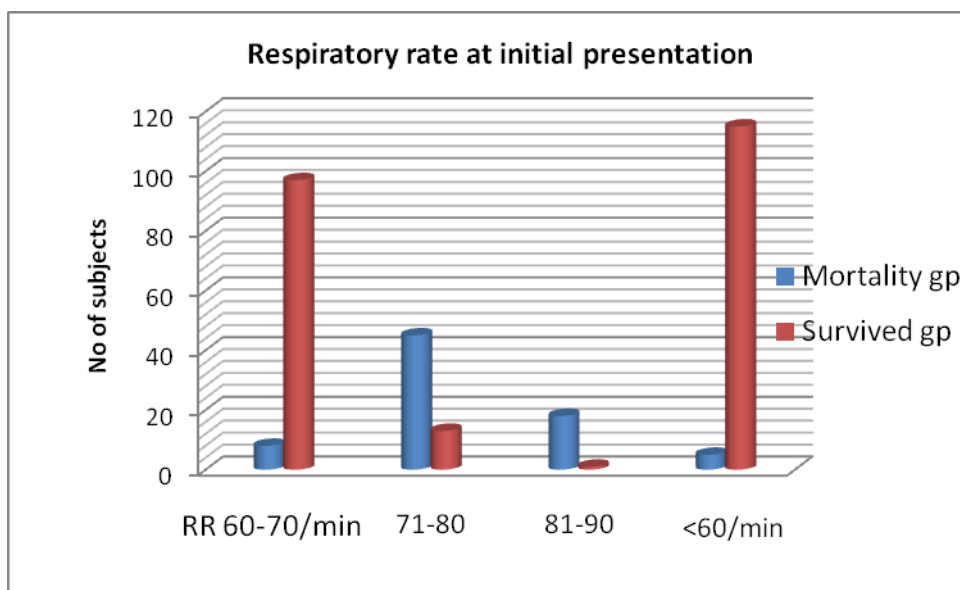
Severe acute malnutrition [SAM] was present in 58(76.3%) cases and 9(3.9%) controls with significant p value and Odd's ratio 77.7[30.9-201.52]. Moderate acute malnutrition [MAM] was observed in 18(23.6%) cases and 142(62.8%) controls. Severe acute malnutrition was 77 times more commonly observed among expired group when compared to recovered group.[Fig 5]



**Figure 5: Bar chart showing weight for height distribution among both groups.**

## Respiratory rate Vs Outcome

Among expired group 2.6% had rate between 60-70/ minute, 59.2% had between 71-80/ minute, 23.6% had rate between 81-90/ minute. Among recovered group 42.9% had between 60-70/ minute, 5.7% had from 71-80/ minute and others had < 60/ minute.[Fig 6]



**Figure 6:** Bar chart showing respiratory rate among both groups.

## Temperature Vs Outcome

Among expired group 36.8% had temperature less than 36.5c and 17.7% among recovered group. 55.2%children had temperature > 37.5c among expired group and 18.1% among recovered group. p value was 0.000, significant.[Table 6]

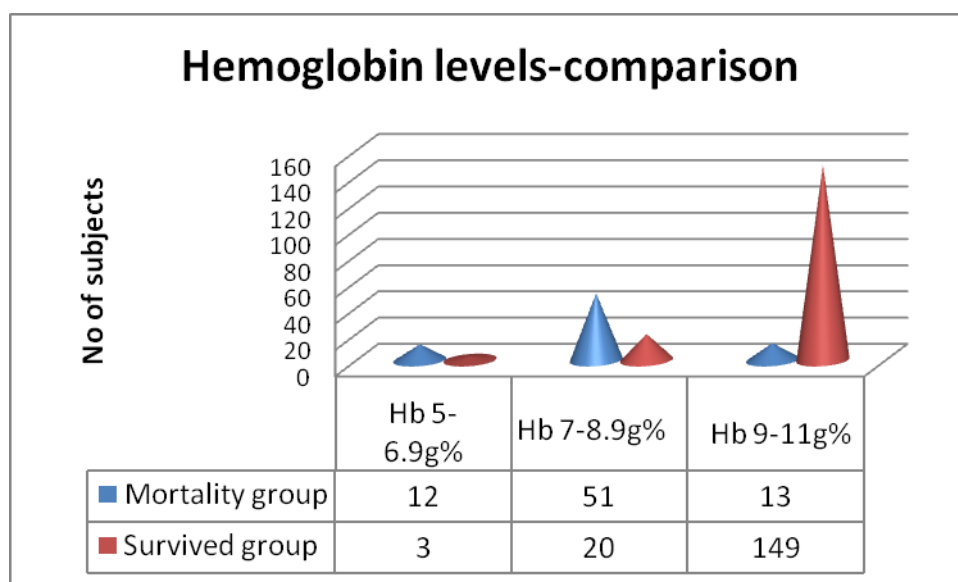
**Table 6: Temperature among expired and recovered groups**

Temperature	Expired group n(%)	Recovered group n(%)	P value
< 36.5 °c	28(36.8)	40(17.6)	0.000
>37.5°c	42(55.2)	4(1.7)	
36.5°c-37.5°c	6(7.8)	182(80.5)	



## Hemoglobin levels among expired and recovered groups

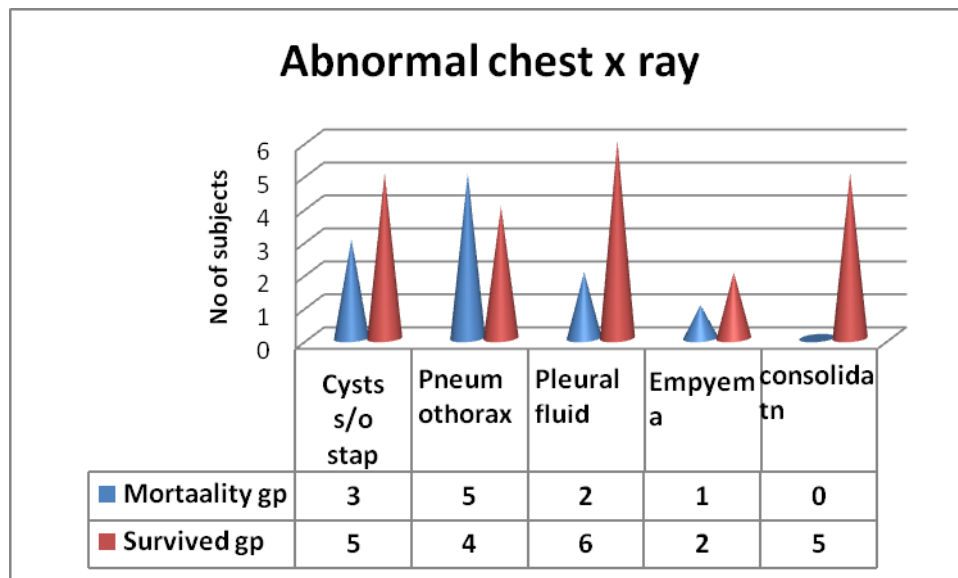
Around 12(15.7%) children had Hb levels in the range of 5-6.9 g %, 51(67%) in the range of 7-8.9 g%, 17% between 9-11 g% among expired group. Whereas in recovered group 65.9 % had values in the range of 9-11g %. P value was 0.000 which was significant.[Fig 7]



**Figure 7: Bar chart showing comparison of hemoglobin levels among both groups.**

### Abnormal chest X ray:

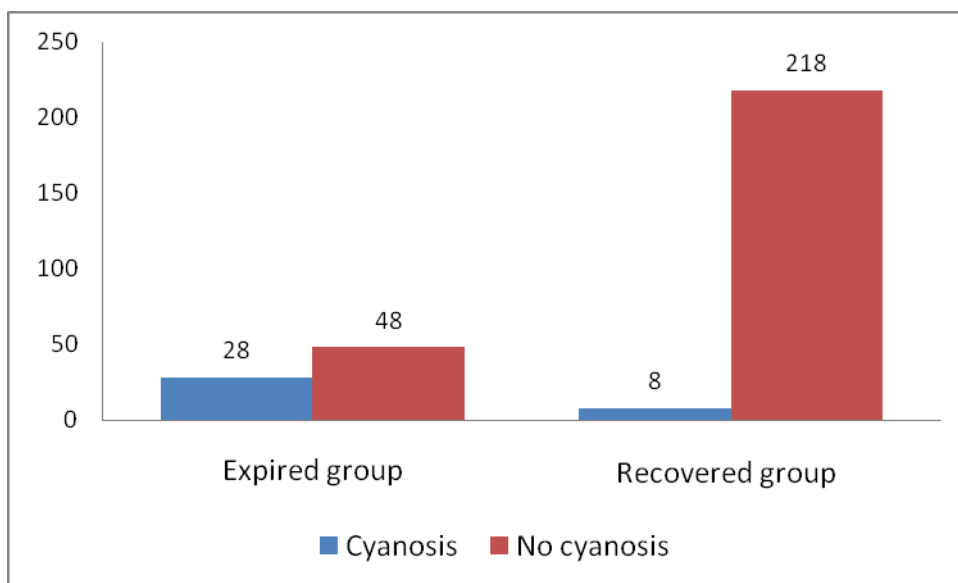
Though chest X ray done in all patients to confirm the diagnosis showed some evidence of pneumonia like focal or diffuse infiltrates/ patches/ bronchopneumoia/ pneumonitis findings like pneumothorax, pleural efusion, consolidation , empyema were named as abnormal as it requires serious monitoring, may require higher antibiotics, potential to cause death. In our study cysts suggestive of staphylococcal infection were present in 3(3.9%) cases and 5(2.2%) controls, pneumothorax in 5(6.5%) cases and 4(1.7%) controls, pleural effusion in 2(2.6%) cases and 6(2.6%) controls, empyema in 1(1.3%) case and 2(0.8%) controls, consolidation in 5(2.2%) controls.[Fig 8]



**Figure 8: Cone chart showing abnormal X rays among both groups**

## CYANOSIS Vs OUTCOME

Presence of cyanosis was noted in 28(36.8%) cases and 8(3.5%) controls with statistical significance and cyanosis was 15 times more commonly observed among expired children. OR(95% CI) is 15.9(6.82-37.03) and p value is 0.000 [Fig 9]



**Figure 9: Bar chart showing comparison of cyanosis among both groups**

**Table 7: GRUNTING Vs OUTCOME**

GRUNTING	OUTCOME		TOTAL
	Expired n(%)	Recovered n(%)	
Present	51(67.1)	16(7.0)	67
Absent	25(32.8)	210(92.9)	235
<b>TOTAL</b>	76	226	302
OR(95% CI) =26.78(13.32-53.82) p value is 0.000			

Around 67.1% children among expired group had grunting on admission and 7.0% among those who recovered. Grunting was 26 times more commonly observed among expired group when compared to those who recovered.[Table 7]

**Table 8: HYPOXEMIA Vs OUTCOME**

HYPOXEMIA	OUTCOME		TOTAL
	Expired n(%)	Recovered n(%)	
Present	69(90.7)	84(37.1)	153
Absent	7(9.2)	142(62.8)	149
<b>TOTAL</b>	76	226	302
<b>OR(95% CI) =16.66(7.32-37.95) p value is 0.000</b>			

Around 90.7% children who expired had hypoxemia on admission and 37.1% among those who recovered. Hypoxemia was 16 times more commonly observed among expired group when compared to those who recovered.[Table 8]

**Table 9: ALTERED SENSORIUM Vs OUTCOME**

<b>ALTERED SENSORIUM</b>	<b>OUTCOME</b>		<b>TOTAL</b>
	<b>Expired n(%)</b>	<b>Recovered n(%)</b>	
Present	73(96)	118(52.2)	191
Absent	3(3.9)	108(47.8)	111
<b>TOTAL</b>	76	226	302
OR(95% CI) =22.27(6.82-72.75) p value is 0.000			

Around 96% children who expired were in altered sensorium and 52.2 among those who recovered. The children expired due to severe/ very severe pneumonia would be 22 times more likely to be with altered sensorium when compared to those who recovered [Table 9]

**Table 10: SHOCK Vs OUTCOME**

SHOCK	OUTCOME		TOTAL
	Expired n(%)	Recovered n(%)	
Present	70(92.1)	86(38.1)	156
Absent	6(7.8)	140(61.9)	146
<b>TOTAL</b>	76	226	302
OR(95% CI) =18.99(7.91-45.6) and p value is 0.000			

Shock was seen among 92.1% children who expired and 38.1% among recovered. Shock was 18.99 times more commonly observed among those expired when compared to those who recovered [Table 10]

**Table 11: CONVUSIONS Vs OUTCOME**

<b>CONVULSIONS</b>	<b>OUTCOME</b>		<b>TOTAL N(%)</b>
	<b>Mortality n(%)</b>	<b>Survived n(%)</b>	
<b>Present</b>	<b>9(11.8)</b>	<b>1(0.4)</b>	<b>10</b>
<b>Absent</b>	<b>67(88.1)</b>	<b>225(99.6)</b>	<b>292</b>
<b>TOTAL</b>	<b>76</b>	<b>226</b>	<b>302</b>
<b>OR(95% CI) =77.69(30.99-201.52) and p value is 0.000</b>			

Convulsions was seen among 11.8% children who expired and 0.4% among who recovered. It was 77 times more commonly observed among those expired whenn compared to those who recovered.[Table 10]



**Table 11: Fluid refractory shock Vs Outcome**

<b>Fluid refractory shock</b>	<b>OUTCOME</b>		<b>TOTAL</b>
	<b>Mortality n(%)</b>	<b>Survived n(%)</b>	
Present	75(98.6)	33(14.6)	108
Absent	1(1.3)	193(85.4)	194
<b>TOTAL</b>	76	226	302
OR(95% CI) =438.64(62.3-8785.3) and p value is 0.000			

Fluid refractory shock was seen among 98.6% children who expired and 14.6% among who recovered. It was 438 times more commonly observed among those expired when compared to those who recovered.[Table 11]

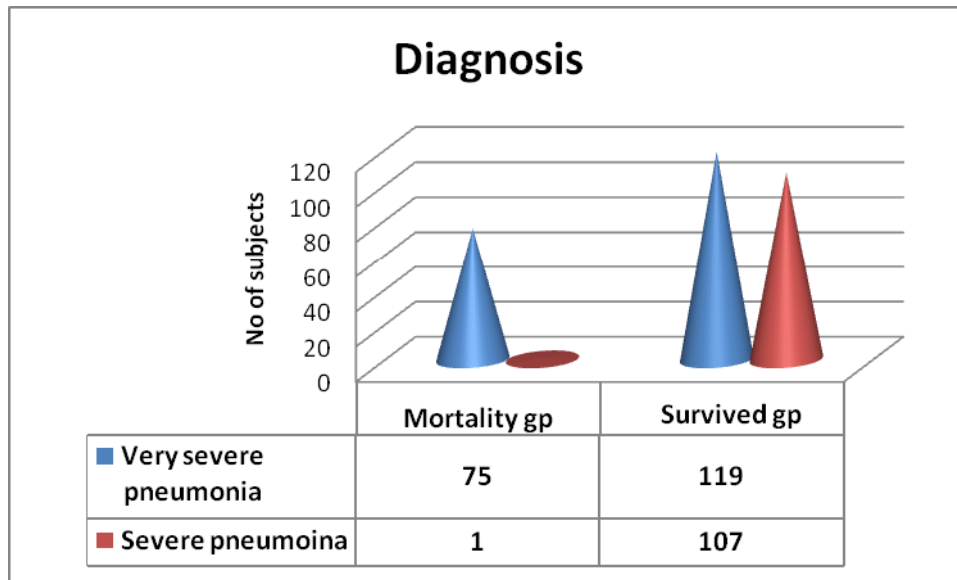
**Table 12: Multiorgan dysfunction Vs Outcome**

<b>Multiorgan dysfunction</b>	<b>OUTCOME</b>		<b>TOTAL</b>
	<b>Mortality n(%)</b>	<b>Survived n(%)</b>	
Present	33(43.4)	2(0.8)	35
Absent	43(56.6)	224(99.1)	267
<b>TOTAL</b>	76	226	302
OR(95% CI) =85.9(19.88-371.64) and p value is 0.000			

Mutiorgan dysfunction was seen among 43.4% children who expired and 0.8% among who recovered. It was 85 times more commonly observed among those expired when compared to those who recovered.[Table 12]

## DIAGNOSIS Vs OUTCOME

Among expired group, 75(98.6%) had very severe pneumonia and 1(1.3%) had severe pneumonia. Among recovered group 119(52.6%) had very severe pneumonia and 107(47.3%) had severe pneumonia. P value was 0.000 which is statistically significant.[Fig 9]



**Figure 9: Cone chart comparing severe and very severe pneumonia among both groups.**

**Table 13: Investigation results among both groups – Univariate analysis**

S no	Variable	Expired group n(%)	Recovered group n(%)	Odd's ratio (95% CI)	P value
1.	Hemoglobin 5-6.9 g% 7-8.9 g% 9- 11 g% >11 g%	12(15.7) 51(67) 13(17) 0	3(1.3) 20(8.8) 149(65.9) 54(23.9)	-	0.000
2.	Total leukocyte count >10,000	54(71)	67(29.6)	5.825(3.17-10.77)	0.000
3.	Blood culture positivity	7(9.2)	2(0.8)	11.15(2.05-79.64)	0.001
4.	Pleural culture	1(1.3)	2(0.8)	1.493(0.05-3-21.36)	1.000

**Table 14: Comparison of risk factors among dead and survived pneumonia groups – Multivariate analysis.**

<b>S.No</b>	<b>Variable</b>	<b>OR</b>	<b>P value</b>
<b>1</b>	Birth weight 2-2.5 kg	56.890	Significant
<b>2</b>	Non breast fed	65.751	Significant
<b>3</b>	Bad child rearing practices	131.828	Significant
<b>4</b>	Not received measles vaccine	14.321	Significant
<b>5</b>	Hypoxemia	65.422	Significant
<b>6</b>	Weight for height $\leq -3$ z score	131.66	Significant
<b>7</b>	Very severe pneumonia as diagnosis	52.453	Significant

## DISCUSSION

Pneumonia, a forgotten killer of community is more common among children less than five years of age. Various risk factors have been identified and studied by a lot in different settings. Yet we are not able to get it under control. This study has been done to study the predictive factors of death in our community, so that we a step towards achievement of under five mortality reduction as majority is contributed by pneumonia.

We did a nested case control study to identify the clinical and laboratory parameters associated with mortality in under five children hospitalized with WHO defined severe and very pneumonia.

A total of 302 children with severe and very severe pneumonia were enrolled in the study. In that 194(64.2%) children had very severe pneumonia and 108(35.8%) children had severe pneumonia which is comparable with the study of Tiewosh et al. 96(31.8%) children were exposed to environmental tobacco smoke, 59(19.5%) children live in indoor polluted homes, 54(17.8%) had received exclusive breast feeding, 73(24.15%) were reared bad child rearing practices, 162(53.6%) were not yet received measles vaccination, 99(32.8%) had low birth weight [2-2.5 kg]

We observed a mortality rate of 25.1% which was comparable to study of Sehgal, Agarwal and Patwari et al<sup>[5,6,7]</sup>. WHO report 2006 on under five deaths highlights that children not breast fed in the first six months of life were five times more prone to suffer from pneumonia. In the present study, lack of exclusive breastfeeding was identified to be an important determinant associated with mortality in severe pneumonia which is comparable with the study of Fonaseca et al, Shah et al, Broor S et al, Victoria CG et al<sup>[19,23,36]</sup>. Breast milk seems to affect the infant's systemic immune system via multiple mechanisms including maturational, anti-inflammatory, immune modulatory and antimicrobial action<sup>[38]</sup>. Changes in immune phenotype after exposure to breast milk, including increase in post-vaccination interferon alpha levels and in natural killer cell numbers could result in prolonged protection against respiratory infections. In addition, there is experimental evidence in animals that maternal milk lymphocytes cross the infant's intestinal wall barrier and enter the circulation<sup>[39]</sup>. It activates the infant's immune system. Anti-inflammatory cytokines such as interleukin-10 and transforming growth factor  $\beta$  are also present in breast milk and taken up by neonatal tissues, in which they are associated with a reduction in inflammatory immune responses<sup>[40]</sup> and enhanced secretory

immunoglobulin A synthesis<sup>[41,42]</sup>. These findings of infant immune responses associated with breastfeeding lend biological credence to the findings in our study, in that breastfeeding could result in a decrease in respiratory infections for many months or even years<sup>[43]</sup>.

Separately pneumonia and malnutrition are two of the biggest killers in childhood. Here severe acute malnutrition was present majority among expired group. Moderate malnutrition was observed in 18(5.9%) cases and 142(47%) controls. Many studies <sup>[45,46]</sup> have already reported acute malnutrition as a significant risk factor associated with mortality. A study done by Christi MJ et al<sup>[47]</sup> searched 16 studies based on association of malnutrition with childhood pneumonia and reported the following results. For severe malnutrition, reported relative risks ranged from 2.9 to 121.2; For moderate malnutrition, relative risks ranged from 1.2 to 36.5, which supports our study finding.

We observed bad child rearing practices was more significantly associated with mortality. As the chances of introducing microorganisms through unhygienic hands are more and the body's defense mechanism to overcome the toxic effect of substances given is poorly developed.



The influence of tobacco smoke on acute lower respiratory tract infections especially on pneumonia morbidity and mortality is undoubtedly significant. Exposure to passive smoking was 3.94 times more among mortality group when compared to survived group. This is comparable to the study of Suzuki<sup>[28]</sup> and study of Laura L Jones<sup>[22]</sup> where the odd's ratio was around 2.

On observation we found that 21(27.6%) of cases and 38(16.5%) of controls lived in an indoor polluted home. A study done by Shah V et al had found indoor smoke as a significant risk factor on univariate analysis <sup>[19]</sup>. Toxic substances released from combustion of wood/ coal/ bio gas/ cow dung/ crop residues increases the acute lower respiratory tract infections either through irritation of the pathway, edema or secondary bacterial infection.

Measles immunization was not given in the majority of expired group which shows that not receiving measles vaccine is associated with significant risk of mortality. This is evidenced by the WHO report 2006 on under five deaths.

Lower maternal education emerged as an important predictor in univariate analysis with severe pneumonia. There are not reports linking maternal education with the outcome of pneumonia. However, maternal knowledge of symptoms of pneumonia is associated with

early recognition and utilization of health care facilities for their children<sup>[44,48]</sup>. It's a well known fact that higher the female literacy rate lower the infant mortality rate and the outstanding example is Kerala state. In our study 22(28.9%) cases and 32(14.2%) controls mother's were illiterate. This is comparable with the study of Shah V [26], as they found low literacy level, a significant factor for mortality with severe pneumonia.

Proportionately more children expired within 24 hours of hospitalization in children who had severe pneumonia, suggesting that these patients could have arrived very late with complications and could have been saved only if intervention could have been done early which is comparable with the study by Banajeh, et al<sup>[13]</sup> **who** reported late hospitalization with cyanosis as one of the significant risk factor for mortality. Overcrowding was noted in 24(31.5%) cases and 69(30.5%) controls which had no statistically significant correlation to our study.

Higher respiratory rate was observed in cases compared to the control group.( $p=0.000$ ). This is comparable with the study of Morley CJ, et al. who reported a respiratory rate of  $> 70$ / minute was associated more significantly with mortality.

Hypothermia and fever both the factors were found to be statistically significant in our study which is comparable with the study done by Neuman,<sup>[50]</sup> et al reported on performing multivariable analyses the factors predicting pneumonia were chest pain, fever > 72 hours, temperature  $\geq 38^{\circ}\text{C}$ , hypoxia and temperature variation.

Among the studied subjects, shock was documented in 92.1% of the cases which shows that the presence of shock significantly increases the risk of mortality. This increased risk could be due to initial hypoxic/ ischemic injury followed with shock correction resulting in reperfusion injury along with damage caused by activation of inflammatory cascade <sup>[32]</sup> .

Altered mental status was observed in 96% of the cases which had significant association with mortality, this is comparable with study of Tiewosh, et al. Cyanosis was observed in 36.8% of the cases, whose presence has got high specificity, a reliable indicator of hypoxemia. In a study done by Shaan et al<sup>[49]</sup> they observed a very high mortality was documented in children with a prolonged illness, severe roentgenogram changes, cyanosis, leukocytosis, hepatomegaly or inability to feed, and there was a trend toward a higher mortality in children with grunting or severe chest indrawing. Our study also had significant association between grunting and mortality.

A trend of leukocytosis was observed among children in mortality group which was similar to findings observed in Shaan<sup>[49]</sup> et al study .

The manifestations in relation to hypoxic injury to brain may vary and presents clinically as restlessness, confusion, irritability, agitation, coma and convulsions. In this study 11.8% of cases developed convulsions, could be as a result of hypoxic injury to brain/ electrolyte disturbances/ manifestation of end organ dysfunction.

Oxygen saturation less than 94% were observed in 90.7% of the cases which is significantly associated with mortality. The risk of death from pneumonia increases significantly when hypoxemia is present<sup>[48,38]</sup>. This is comparable with the study of Djelantik IG where the risk of mortality is 5.6 times more when hypoxemia present at admission.

Totally 9(2.9%) children had growth in blood culture, six samples grew staphylococcus aureus and 3 samples grew klebsiella pneumoniae. Out of 3 positive pleural cultures 2 samples grew staphylococcus aureus and 1 sample grew streptococcus pneumoniae.

We observed that low birth weight between 2 kg -2.49 kg, non breast fed babies, those mother following bad child rearing practices, children not yet immunized with measles vaccine, weight for height  $\leq$

-3 Z score (severe acute malnutrition), hypoxemia at first contact with medical care were the significant predictive factors associated with mortality due to severe and very severe pneumonia on multivariate analysis.

Variables shown to be significantly associated with mortality when considered independently in univariate analysis were age less than 6 months, exposure to passive smoking, indoor smoke, living in crowded homes, increased respiratory rate, temperature variation, mothers education, sepsis, shock, altered sensorium, cyanosis, grunting, convulsions, weight for height less than or equal to – 3 Z score, hemoglobin levels between 7-8.9 g%, leukocytosis, positive blood culture, fluid refractory shock, multiorgan dysfunction, very severe pneumonia as diagnosis. These variables became non-significant in a multivariate model. This does not necessarily mean loss of information but implies that the non-significant variables are explaining the same or less variability in severity as the significant variables and are therefore redundant.

**Strengths of present study** include prospective nature of this study and that the patients were enrolled and multiple factors were monitored daily till the end point occurred.

**Limitations of the study** are small sample size, controls were not matched exactly. Blood culture positivity was only 2.9%.

## CONCLUSION

In a study of severe and very severe pneumonia in children aged 2 to < 60 months in an urban tertiary referral care centre the following emerged as significant factors for mortality

1. Low birth weight between 2- 2.49 kg
2. Severe acute malnutrition
3. Children exposed to bad child rearing practices
4. Non breast fed status
5. Not immunized with measles vaccine
6. Hypoxemia at first contact with medical care

Preferably such children should be admitted in pediatric intensive care unit for more aggressive monitoring and management that could reduce their mortality.

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## **PREDICTORS OF MORTALITY IN PNEUMONIA**

**S.NO.**

**DATE:**

**IP NO:**

**NAME:**

**AGE:**

**Weight for height:**

**DOA:**

**DOD/ABS/AMA/DEATH:**

**Time of arrival:**

### **SYMPTOMS**

### **DURATION**

1.FEVER

8.CHEST PAIN

2.COUGH

9.CYANOSIS

3.FAST BREATHING

10.POOR FEEDING

4.BREATHLESSNESS

11.VOMITING

5.GRUNTING

12.ALTERED SENSORIUM

6.NOISY BREATHING

13.POOR FEEDING



## **FACTORS**

- |                    |                                |
|--------------------|--------------------------------|
| 1.MOTHER EDUCATION | 7.FIRST MED CONTACT-OFI        |
| 2.PERSON/ROOM..... | 8.IMMUNIZATN Ms / Hib / Pneumc |
| 3.INDOOR SMOKE     | Y / N LPG/PUMP/ WOOD STOVE     |
| 4.FATHER SMOKES    | Y / N CIGAR / BEEDI            |
| 5.BIRTH WT         | 9. BAD CRP-Y / N               |
| 6.EBF .....        | Y/N                            |

## **SIGNS**

- |                           |                       |
|---------------------------|-----------------------|
| 1.TEMP                    | 6.CYANOSIS Y / N      |
| 2.RR                      | 7.NASAL FLARING Y / N |
| 3.HR                      | 8.GRUNTING Y/N        |
| 4.PERFUSION -Shock/Normal | 9.CREPS/WHEEZE Y / N  |
| 5.RETRACTIONS Y / N       | 10.SpO2 in RA         |
| 6.ALTERED SENSORIUM Y/ N  | 11.CONVULSIONS Y / N  |

## **INVESTIGATIONS**

- |                    |                    |
|--------------------|--------------------|
| 1.Hb               | 6.CXR DATE         |
| 2.TC               | REPORT             |
| 3.BLD CULTURE NG/G | 7. Serum bilirubin |
| 4.CRP P/N          | 8. SGOT/ SGPT      |
| 5.PLEURAL FLD CUL  | 9. Sr creatinine   |

**TREATMENT**

1.O2	Y / N
2.ANTIBIOTICS	ORAL/ IV
3.IVF	Y / N
4.VENTILATED	Y / N
5.BLOOD TRANSFUSION	Y / N

**COMPLICATIONS**

1.FLUID REFRACTORY SHOCK	Y / N
2.PNEUMOTHROAX	Y / N
3.PLEURAL EFFUSION	Y / N
4.EMPYEMA	Y / N
5.ENCEPHALOPATHY	Y / N
6. SEPSIS/ MODS	Y / N
7. ARDS	Y / N

WHO diagnosis.....

**OUTCOME****IMPROVED/DEATH**

## தகவல் அளிக்கப்பட்ட ஒப்புதல் படிவம்

எனது குழந்தைக்கு தீவிரமான மற்றும் மிகவும் தீவிரமான நிமோனியா நோயால் பாதிக்கப்பட்டிருப்பதை மருத்துவர் மூலம் தெரிவிக்கப்பட்டது.

இந்த ஆய்வு பற்றி எனக்கு விளக்கமாக எனது தாய்மொழியில் தெரிவிக்கப்பட்டது. இந்த ஆய்வில் பங்கெடுத்துக் கொள்வதால் குழந்தைக்கு ஏற்படக்கூடிய அபாயங்கள் மற்றும் நன்மைகள் பற்றி எனக்கு விவரமாக தெரிவிக்கப்பட்டது. இந்த ஆய்வில் எனது குழந்தை பங்கெடுத்துக் கொள்ள முழு மனதுடன் சம்மதிக்கிறேன். கேள்விகள் கேட்பதற்கு எனக்கு வாய்ப்பளிக்கப்பட்டது.

இந்த ஆய்விலிருந்து கிடைக்கும் முடிவுகளை பயன்படுத்துபவரை கட்டுப்படுத்தாமலிருக்க நான் சம்மதிக்கிறேன்.

குழந்தையின் பெயர் -

குழந்தையின் பெற்றோர் / -

கண்காணிப்பாளர் பெயர்

குழந்தையின் பெற்றோர் / -

கண்காணிப்பாளர் கையெழுத்து

தேதி -

எழுதப்படிக்கத் தெரியாத -

பெற்றோர் / கண்காணிப்பாளர்

கைவிரல் ரேகை

சாட்சியின் பெயர் -

சாட்சியின் கையெழுத்து -

தேதி -

ஆய்வாளர் / ஆய்வு மருத்துவர் -

பெயர்

ஆய்வாளர் / ஆய்வு

மருத்துவர் கையெழுத்து -